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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,824	05/23/2001	C. Alexander Turner JR.	LEX-0181-USA	8987

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EXAMINER

RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 05/14/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/863,824

Applicant(s)

TURNER ET AL.

Examiner

Delia M. Ramirez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 5 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 and 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-3 are pending.

Applicant's election with traverse of Group I, claims 1-3 drawn in part to the polynucleotide encoding the protein of SEQ ID NO: 2, in Paper No. 8, filed on 2/27/2002 and submission of an IDS in Paper No. 9, filed on 4/23/2002 are acknowledged.

Applicant's traverse is on the ground(s) that the polynucleotides of SEQ ID NO: 1, 3, and 5 and the corresponding polypeptides (SEQ ID NO: 2, 4, and 6) are all encoded by a common genetic locus and that Groups I-III are all drawn to highly related sequences that share a common nexus of invention. Further, Applicants assert that all the instant polynucleotides encode splice variants of a novel human thrombospondin-like protein and share substantial structural features.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the restriction requirement. While the activity of the polypeptides encoded by the polynucleotides of the instant invention, as Applicants assert, may be similar (thrombospondin activity), as indicated in previous Office Action Paper No. 6, mailed on 1/11/2002, each one of the polynucleotides of the instant invention comprise a different structure and encode a different protein with unrelated amino acid sequences. Therefore, each polypeptide, and its corresponding polynucleotide, is a patentably distinct invention. In addition, the search of each invention would impose an undue burden on the Office since the search is not co-extensive.

The requirement is deemed proper and therefore is made FINAL.

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Claims 4-5 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. In addition, claims 1-3 will be examined only as they relate to the elected invention, which is the polynucleotide encoding the polypeptide of SEQ ID NO: 2, therefore Applicants are requested to amend the claims accordingly.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/206,415 filed on 5/23/2000.

Claim Objections

2. Claim 1 is objected to because of the following informalities: the language “comprising at a nucleotide” should be “comprising a nucleotide”. Appropriate correction is required.

3. Claim 1 objected to because of the following informalities: for clarity, the term “drawn” should be replaced with “selected”. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

5. Applicants assert that the polypeptides encoded by the polynucleotides of the instant invention share structural similarity to several proteins including, but not limited to, mammalian

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thrombospondins, semaphorins, metalloproteinases, and serine palmitoyltransferase. (page 16, lines 5-13). Further, the specification discloses that thrombospondins are extracellular proteins that have been implicated in blood clotting, angiogenesis, diabetes, inflammation, wound healing, and cancer (page 1, lines 23-25). The specification also discloses that the polynucleotides of the instant invention can be used to screen collections of genetic material from patients who have a particular condition (page 7, lines 26-29). Other uses for the polypeptide or the corresponding polynucleotide include protein therapeutics, identification of related polypeptides/polynucleotides, and screening of pharmaceutical reagents useful in the treatment of diseases (page 19, lines 1-14).

6. However, based upon Applicant's disclosure, the claimed invention does not meet the utility requirement for the following reasons. First, if one assumes that the asserted function of the polypeptide of the instant invention is that of a thrombospondin, one cannot determine which type of thrombospondin is being encoded by the polynucleotide of the instant invention (SEQ ID NO: 1) or what is the function of the polypeptide. Therefore, no specific use has been disclosed. Thrombospondins, as known in the art, belong to a family of at least 5 members in vertebrates, each with diverse functions. Therefore, one of skill in the art cannot determine the actual function of the protein (SEQ ID NO: 2) encoded by the polynucleotide (SEQ ID NO: 1) of the instant invention. In addition, neither Applicant's disclosure, nor the state of the art at the time the invention was made provides guidance as to what the function of the polypeptide of SEQ ID NO: 2 is. No working examples have been provided either. No disclosure of critical structural elements which would indicate the type of thrombospondin being encoded by the polynucleotide (SEQ ID NO: 1) of the instant application is provided.

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7. Second, Applicant has provided no supporting empirical evidence that the polypeptide of SEQ ID NO:2 encoded by the nucleic acid sequence of SEQ ID NO:1 is a thrombospondin. The predicted function of the polypeptide of SEQ ID NO:2 is based solely upon sequence alignment analysis. The state of the art suggests that sequence identity alone is insufficient to accurately predict a polypeptide's asserted utility, and that sequence comparison alone should not be used to determine a protein's function (see for example, Bork *Genome Research*, 10:348-400, 2000). Bork teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Applicant's own specification discloses that the polypeptide encoded by the polynucleotide of the instant application share structural similarity with several proteins of different function (see discussion above and attached sequence alignments). The closest homolog found (SPTREMBL accession number O95432, May 1, 1999) is a serine palmitoyltransferase having 36.8% sequence identity to SEQ ID NO: 2. A human thrombospondin (PIR accession number TSHUP1, August 23, 1987) is 5% sequence identical to the polypeptide of SEQ ID NO: 2 whereas a procollagen I N-proteinase (PIR accession number T18517, October 15, 1999) presents 4.9% sequence identity to the polypeptide of the instant application. Since the function and identity of the polypeptide of SEQ ID NO: 2 remain unknown, there is no well-established utility for the polynucleotide of SEQ ID NO:1.

8. Applicant's asserted utility for the polypeptide of SEQ ID NO: 2 (thrombospondin), particularly in view of a lack of knowledge as to the type of thrombospondin and its function, constitutes a utility that requires further research to identify or reasonably confirm a "real world" context of use. See e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility". An assay that detects the presence of an

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agent that has a stated correlation to a predisposition to the onset of a specific disease condition would be considered a "substantial utility" in the context of identifying potential candidates for preventive measures. Here the polynucleotide and corresponding polypeptide are suitable only for additional research. Thus, for the reasons set forth, the claimed polynucleotide does not have a real-world use and hence lack utility for the reasons set forth above.

9. Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. In case Applicant overcomes this utility rejection by providing convincing evidence in response to this Office Action, the following rejections will apply:

Claim Rejections - 35 USC § 112, Second Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 2 is indefinite in the recitation of "an isolated nucleic acid molecule comprising a nucleotide sequence that: (a)....; and (b) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof." for the following reasons. First, it is

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not clear how a sequence can hybridize to another sequence since hybridization, as known in the art, occurs between nucleic acid molecules. Second, the term “complement” renders the claim indefinite because it is unclear which “complements” are encompassed by the claims. Fragments of any size which are complementary to the polynucleotides claimed can be considered as “complements”. Applicants have not defined the term “complement”, as it relates to size, in the specification either. If applicants wish to claim the entire complementary sequence, it is suggested that the term “complement” be replaced with “complete complement”.

14. Claim 2 is indefinite in the recitation of “hybridizes under stringent conditions” absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. Applicants have disclosed several conditions in the specification (page 4, lines 14-25) as stringent conditions. It is suggested that if Applicant’s intended conditions are highly stringent, the claims be amended to include the experimental conditions disclosed by Applicants in page 4, lines 14-17, since these are recognized as highly stringent conditions in the art (wash conditions 0.1xSSC, 0.1% SDS at 68 °C). Correction is required.

Conclusion

15. No claim is in condition for allowance.

16. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

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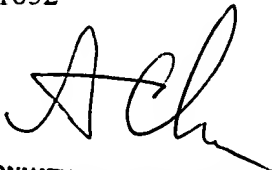
17. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
May 9, 2002


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